REMARKS

Applicant has amended the Specification. The specific changes to the Specification are shown above in the Amendments to the Specification, wherein the insertions are underlined and the ~~deletions are stricken through~~. Applicant has amended Claims 1 and 7, and canceled Claims 26-29. Thus, Claims 1-25 are presented for examination. The specific changes to the amended claims are shown above in the Amendments to the Claims, wherein the insertions are underlined and the ~~deletions are stricken through~~. Applicant responds below to rejections made by the Examiner in the Office Action of June 22, 2006.

I. Interview Summary

A telephonic interview was conducted on Wednesday, September 27, 2006. The participants in the interview were Examiners Larry Helms and Lynn Bristol on behalf of the Patent Office, and attorneys Mike Fuller and Erik Anderson on behalf of Applicant. During the interview, the participants discussed the pending claims and the cited art, with particular reference to the claim term "adjusting the conditions of the cell media to activate at least one endogenous enzyme that cleaves said antibodies." No exhibit was shown. No final agreement was reached.

II. Election/Restrictions

Applicant elected Group I (Claim 1-25) in the Response to Restriction Requirement filed on May 23, 2006. Applicant has cancelled the claims of Group II (Claims 26-29) without prejudice to their continued prosecution in one or more divisional, continuation, or continuation-in-part applications. Applicant respectfully submits that Claim 1 is generic to the species of Claims 8 and 9, all of which were included in Restriction Group I. Although Claims 8 and 9 recite species of endogenous antibody-cleaving enzymes that were not elected, Applicant respectfully submits that Claims 8 and 9 should be rejoined once the underlying base claim, Claim 1, is deemed allowable.

III. Objections to the Specification

The Examiner has objected to the abstract and page 2 of the specification for including the attorney docket number. Although the Examiner cites "37 C.F.R. 1.171(f)," Applicant believes that the Examiner intended to refer to 37 C.F.R. § 1.71 (f), which states:

> The specification must commence on a separate sheet. Each sheet including part of the specification may not include other parts of the application or other information. The claim(s), abstract and sequence listing (if any) should not be included on a sheet including any other part of the application.

Applicant respectfully submits that an attorney docket number, in this case consisting of about a dozen typographical characters, should not be deemed an "other part[] of the application," or "other information" under this provision, and further submits that affixing an attorney docket number on patent application documents is a generally accepted practice in the PTO.

The Examiner has also noted the use of trademarks (e.g. XenoMouse™) in the application, indicating that the mark should be capitalized wherever it appears and be accompanied by generic terminology. Applicant has amended the specification to place the mark in all capital letters and indicate that XENOMOUSE® is a registered trademark. Applicant has also included generic terminology in connection with the mark, such as "strains of mice," as appropriate.

Applicant respectfully requests that the objections to the Specification be withdrawn.

IV. Claim Objections

The Examiner has objected to Claim 11 for being drawn to non-elected subject matter. Applicant respectfully submits that Claim 11 is included in Group I, which was elected by Applicant on May 23, 2006 for prosecution. Although Claim 11 recites cell lines in addition to the elected species AA, Chinese hamster ovary cells, Applicant respectfully submits that the objection is improper because the additional cell lines do not represent non-elected groups, and that Claim 11 should be allowable once the underlying base claim, Claim 1, is deemed allowable. Applicant respectfully requests that the objection be withdrawn.

V. Rejections under 35 U.S.C. § 112

The Examiner has rejected Claim 1 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to point out and distinctly claim the subject matter which Applicant regards as the invention. Specifically, the Examiner states that Claim 1 is indefinite for the recitation of "adjusting the conditions of the cell media" because it is unclear whether the adjusting step can be adding an enzyme or adding a culture medium containing an enzyme, or whether chemical modification or a critical time period for enzyme activation is required.

Applicant respectfully submits that the full limitation relating to "adjusting" provides the definiteness required by § 112. The full claim limitation is "adjusting the conditions of the cell media to activate at least one endogenous enzyme that cleaves said antibodies." Accordingly, the limitation requires that conditions be adjusted in the cell media (in which the cell line is growing), and that at least one endogenous enzyme (already in the cell media) be activated as a result of "adjusting the conditions." Accordingly, such "adjusting" is not met by merely adding a new enzyme to the cell media. Further, examples of techniques for adjusting the conditions of cell media are discussed in paragraphs [0042]-[0044] and [0050] of the present specification.

The Examiner has also rejected Claim 12 under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement. Specifically, the Examiner states that it is unclear if the cell line CHO-DG44 is known and publicly available, or can be reproducibly isolated without undue experimentation. Applicant respectfully submits that CHO-DG44 is a known and commercially available cell line. Applicant encloses herewith advertising information from two commercial sources of CHO-DG44 cells (Irvine Scientific of Santa Ana, CA and Xcellerex, Inc. of Marlborough, MA), as well as search results for "CHO-DG44" on www.pubmed.gov, showing eighteen documents that contain the term, and thus describe these cells. Because the cell line is known and commercially available, Applicant respectfully submits that no deposit is necessary.

The Examiner has also rejected Claims 1, 3-7, and 10-18 under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement. Specifically, the Examiner states "the specification, while being enabling for making and using Fab, Fab', $F(ab')_2$, Fv, and single chain antibodies that compete with the intact antibody for specific binding, does not reasonably provide enablement for making or using just any antibody fragments that do not retain binding activity or which cannot be used in immunoassays, immunotherapeutics or immunodiagnostics." Applicant respectfully submits that the claims, as amended, are directed to a method of generating "antigen-binding" fragments. Support for the amendment can be found, for example, in the present specification at paragraphs [0016]-[0019], which discuss various antigen-binding fragments. Applicant respectfully submits that the amendment overcomes the rejection.

Accordingly, Applicant respectfully requests withdrawal of the § 112 rejections.

VI. Claim Rejections - 35 U.S.C. § 103

The Examiner has rejected Claims 1-7, 10, 11, 13, and 16-18 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Takai et al. (Biosci. Biotechnol. Biochem. 65:1082-1089 (2001)) in view of Parham (J. Immunol. 131:2895-2902 (1983)).

Takai et al. teach transfected CHO cells for producing antibodies, and the digestion of antibodies with papain to generate Fab fragments. In Takai et al., the papain is immobilized on beaded agarose, and added specifically for digesting the antibodies produced by the CHO cells. Takai et al. do not disclose *adjusting conditions of the cell media to activate at least one endogenous enzyme* as recited in the claims.

Parham teaches generating antibody fragments by adding pepsin, but, like Takai et al., does not teach *adjusting conditions of the cell media to activate at least one endogenous enzyme* that cleaves antibodies.

As the Examiner has indicated, the Examiner previously interpreted Claim 1 such that "adjusting the conditions of the cell media" could be satisfied by adding a proteolytic enzyme to the antibody for cleavage into fragments. However, as Applicant discussed above, a full reading of the claim does not permit such an interpretation. The full claim limitation is "adjusting the conditions of the cell media to activate at least one endogenous enzyme that cleaves said antibodies." Accordingly, this claim element is not taught by a reference that discloses merely adding a new enzyme to the cell media.

Accordingly, Applicant respectfully submits that neither Takai et al. or Parham disclose or fairly suggest adjusting cell media conditions to activate an endogenous enzyme.

The Examiner has also rejected Claims 1, 14, and 15 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Takai et al. and Parham, further in view of Zhang et al. (Cytotechnology 16:147-150 (1994)) and Shifferli et al. (Focus 21:16-17 (1999)). The Examiner cites Zhang et al. for the disclosure of adding peptone to hybridoma medium to boost antibody production and Shifferli et al. for the disclosure that CD-CHO medium is optimized for growth and expression of recombinant proteins by transfected cells. However, neither Zhang et al. nor Shifferli et al. rectify the principal shortcomings of Takai et al. and Parham, which is that the references do not disclose or fairly suggest adjusting cell media conditions to activate an endogenous enzyme.

The Examiner has also rejected Claims 19, 21, 24, and 25 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Takai et al. and Parham. Claim 19 includes the step of "activating endogenous aspartyl enzyme activity in said cell media, wherein said activation results in cleavage of said recombinant antibody into $F(ab')_2$ fragments." As discussed above, Takai et al. and Parham teach cleaving antibodies by adding enzymes, but do not teach or fairly suggest activating an endogenous enzyme in the cell media.

The Examiner has also rejected Claims 19 and 20 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Takai et al. and Parham, further in view of Shifferli et al. Again, the Examiner cites Shifferli et al. for the disclosure of CD-CHO medium for making recombinant proteins. However, none of the art of record discloses or fairly suggests activating endogenous aspartyl enzyme activity in cell media.

The Examiner has also rejected Claims 19, 22, and 23 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Takai et al. and Parham, further in view of Mason et al. (Protein Expression and Purification 23:45-54 (2001)). The Examiner cites Mason et al. for the disclosure of E64 as a "generic cystein proteinase inhibitor." Notably, however, Mason et al. does not rectify the principal shortcoming of Takai et al. and Parham, which is that the references do not disclose or fairly suggest activating endogenous aspartyl enzyme activity in cell media.

For the foregoing reasons, Applicant respectfully requests that the § 103 rejections be withdrawn.

CONCLUSION

Applicant has endeavored to address all of the Examiner's concerns as expressed in the outstanding Office Action. Accordingly, amendments to the claims, the reasons therefor, and arguments in support of the patentability of the pending claim set are presented above. Any claim amendments which are not specifically discussed in the above remarks are made in order to improve the clarity of claim language, to correct grammatical mistakes or ambiguities, and to otherwise improve the capacity of the claims to particularly and distinctly point out the invention to those of skill in the art.

In light of the above amendments and remarks, reconsideration and withdrawal of the outstanding rejections is respectfully requested. If the Examiner has any questions which may be answered by telephone, the Examiner is invited to call the undersigned directly.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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Dated: 10/12/2006

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